III. REMARKS

Reconsideration of the present application as amended is respectfully requested.

A. Status Of The Claims

Claims 37, 40-47, and 49 are pending in this application. Claim 37 has been amended without prejudice to include the limitation of claim 48 and to correct a typographical error in the spelling of cyclazocine. It is respectfully submitted that no new matter has been added by virtue of this amendment.

B. Rejections under 35 USC § 103(a)

Claim 37 and 40-47 were rejected under 35 U.S.C. 103(a) "as being obvious over Crain et al (U.S. Patent No. 5,767,125) in view of Reder et al (U.S. Patent No. 5,968,547)." The Examiner states that "[i]t would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the analgesic combination of Crain et al using the transdermal delivery system of Reder et al because Crain et al's analgesic combination can be administered using any transdermal delivery system, because Reder et al's transdermal system is used to deliver analogous compounds for the same analgesic purpose, and because use of Reder et al's transdermal system will permit long-time pain relief with minimal intrusion to the patient."

Claims 48 and 49 were rejected under 35 U.S.C. 103(a) "as being obvious over Crain et al (U.S. Patent No. 5,767,125) in view of Reder et al (U.S. Patent No. 5,968,547) as applied against claims 37 and 40-47 above, and further in view of the WO Patent Application 00/01377 or Simon (U.S. Patent No. 6,103,258)." The Examiner states that "Crain et al and Reder et al do not teach releasing the opioid agonist and antagonist at substantially proportionate rates." The Examiner further states that "[t]he WO Patent Application '377 teaches co-administration of opioid agonists and antagonists by intramuscular, intravenous, nasal, oral, sublingual or transdermal methods, recognizes that the individual components can have different pharmacokinetic profiles and different in vivo life spans, and teaches providing a controlled release matrix or coating to the shorter-acting component so that its pharmacokinetic profile

better matches the profile of the longer-acting component, i.e., so that their release rates are proportional." The Examiner concludes that "[i]t would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to provide controlled release matrices or coatings as taught by the WO Patent Application '377 and Simon to the agonist or antagonist of Crain et al as modified above by Reder et al so that the problem of different pharmacokinetic profiles and in vivo lifespans is avoided."

In response, claim 37 has been amended without prejudice to incorporate the limitation of claim 48. Therefore, the rejections of previous claims 37 and 40-47 are now moot.

The rejection of previous claims 48 and 49 based on the combination of Crain et al in view of Reder et al and further in view of either of the Simon references (WO Patent Application No. 00/01377 or U.S. Patent No. 6,103,258) is respectfully traversed.

The Examiner is directed to Section 2143.01 of the 8th Edition of the MPEP which states the following:

> "*If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.*" In re Gordon, 733 F.2d 900, 221 USPQ 1123 (Fed. Cir. 1984).

It is respectfully submitted that the Simon references are directed to the use of kappa opioid antagonists such as nalmefene. The Simon references fail in the very least to teach, hint or suggest an opioid antagonist selected from the group consisting of naloxone, naltrexone, cyclazocine, levallorphan and pharmaceutically acceptable salts thereof, as recited in claim 37. Further, it is respectfully submitted that the Simon references teach away from other antagonists, e.g., at column 2, lines 48-52 (of the '258 patent), which states as follows:

> *The present author describes in the application for U.S. Patent No. 5,783,583 in great detail the unique characteristics common only to the opioid antagonist nalmefene, which sets nalmefene apart from other opioid*

antagonists such as, for example, naloxone and naltrexone.

and at column 4, lines 38-47 (of the '258 patent), which states as follows:

> *Other investigators have contemplated preparations of opioid agonists in combination with naloxone. However, as '538 clearly shows, nalmefene and naloxone are not analogous compounds. Therefore, the present invention would not be obvious to one skilled in the art simply because naloxone has previously been combined with opioid agonists. In fact, because of naloxone's opioid receptor subtype binding profile, it could not exert the positive opioid effects as nalmefene at similar doses, as taught in the present invention.*

Therefore, it is respectfully submitted that utilizing the Simon references to arrive at an invention which does not comprise nalmefene would result in a modification which would render the Simon references unsatisfactory for its intended purpose. Accordingly, it is respectfully submitted that the rejection of the claims over a combination Crain et al. and Reder et al. with Simon or WO 00/01377, be removed.

D. Conclusion

It is now believed that the above-referenced rejections have been obviated and it is respectfully requested that the rejections be withdrawn. It is believed that all claims are now in condition for allowance.

According to currently recommended Patent Office policy the Examiner is requested to contact the undersigned in the event that a telephonic interview will advance the prosecution of this application.

An early and favorable action is earnestly solicited.

Respectfully submitted,

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